THE 21-GENE RECURRENCE SCORE:

BEATSON WEST OF SCOTLAND CANCER CENTRE EXPERIENCE

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03/02/2017
THE 21-GENE RECURRENCE SCORE:

Beatson West of Scotland Cancer Centre Experience

Today’s talk:

- Background on Oncotype Dx RS
- Available guidelines
- 2016 Beatson’s West of Scotland Data
- Discussion
EARLY BREAST CANCER

- Surgery
- Targeted tx
- Radiotherapy
- Endocrine
- Chemotherapy
Survival

Quality of Life

Cost

Side effects
TREATMENT DECISIONS ARE DRIVEN BY BOTH PROGNOSTIC AND PREDICTIVE FACTORS

Prognostic factors

- Nodal status
- Tumor size
- HER2
- ER/PR

Predictive factors for adjuvant therapy

- ER/PR
- HER2
Treatment decisions are driven by both prognostic and predictive factors.

**Prognostic factors**
- Nodal status
- Tumor size
- HER2
- ER/PR
- Oncotype DX® assay
- Other multi-gene signature assays

**Predictive factors for adjuvant therapy**
- ER/PR
- HER2
- Oncotype DX assay
ONCOTYPE DX

- PCR based expression assay measures expression of 21 gene.

- The output is the “Recurrence Score” RS

- Continues variable that predicts risk of distant recurrence at 10 years following Tamoxifen

- 3 risk groups: low, intermediate, high

- Intermediate risk 10%-20% of distant metastasis over 10 years
PRACTICING PRECISION MEDICINE
THE ONCOTYPE DX® BREAST CANCER ASSAY

16 Breast Cancer-Related Genes

- **Estrogen**
  - ER
  - PR
  - Bcl2
  - SCUBE2

- **Proliferation**
  - Ki-67
  - STK15
  - Survivin
  - Cyclin B1
  - MYBL2

- **HER2**
  - GRB7
  - HER2

- **Invasion**
  - Stromelysin 3
  - Cathepsin L2

- **Others**
  - CD68
  - GSTM1
  - BAG1

5 Reference Genes

- Beta-actin
- GAPDH
- RPLPO
- GUS
- TFRC

Recurrence Score

The Oncotype DX Breast Cancer Assay uses RT-PCR to determine the expression of a panel of 21 genes in tumor tissue. The Recurrence Score result is calculated from the gene expression results and ranges from 0-100.

The findings are applicable to women who have stage I or II node negative (N-), estrogen receptor positive (ER+) breast cancer, and will be treated with 5 years of tamoxifen (Tam). It is unknown whether the findings apply to other patients outside these criteria.

Clinical Experience: The following results are from a clinical validation study that included 668 patients from the NSABP B-14 study. The study included female patients with stage I or II, N-, ER+ breast cancer treated with 5 years of Tam.

Prognosis: 10-Year Risk of Distant Recurrence after 5 Years of Tam, Based on the Recurrence Score Result (from NSABP B-14)

10-Year Risk of Distant Recurrence

Tam Alone

7%  (95% CI: 4%-9%)

- Low Risk Group: Average 7%
- Intermediate Risk Group: Average 14%
- High Risk Group: Average 37%
The findings are applicable to women who have stage I or II node negative (N−), estrogen receptor positive (ER+) breast cancer and will be treated with 5 years of tamoxifen (tam). It is unknown whether the findings apply to other patients outside these criteria.

Clinical Experience: The following results are from a clinical validation study that included 651 patients from the NSABP B-20 study. The study included female patients with stage I or II, N−, ER+ breast cancer. Patients were randomized to either tam alone or tam plus CMF or MF chemotherapy. For patients in the pre-specified group with Recurrence Score results ≥ 31, the group average 10-year risks (95% CI) of distant recurrence were 40% (25%, 54%) for tam alone and 12% (6%, 18%) for tam + CMF/MF.¹

Prediction of Chemotherapy Benefit after 5 Years of Tam, Based on the Recurrence Score Result (from NSABP B-20)
Quantitative Single-Gene Report

Regulation: RX00014
Specimen Received: 30-Sep-2012
Date Reported:

The Oncotype DX® assay uses RT-PCR to determine the RNA expression of the genes below. These results may differ from estrogen receptor (ER), progesterone receptor (PR), or human epidermal growth factor receptor 2 (HER2) results reported using other methods or reported by other laboratories. The ER, PR, and HER2 Scores are also included in the calculation of the Recurrence Score result.

**ER Score**
- **Positive**: 7.5
- Range: Patient
  - Negative < 6.5
  - Positive ≥ 6.5

The ER Score positive/negative cut-off of 6.5 units was validated from a study of 761 samples using the 1D5 antibody (immunohistochemistry) and 607 samples using the SP1 antibody (immunohistochemistry). The standard deviation for the ER Score is less than 0.5 units.

**Clinical Experience:**
For ER+ breast cancer, the magnitude of tamoxifen benefit increases as the ER Score increases from 6.5 to 21.2. The clinical experience is an important consideration for patients who received 5 years of tamoxifen treatment and take into account the magnitude of tamoxifen benefit indicated by the ER Score.

**PR Score**
- **Positive**: 6.1
- Range: Patient
  - Negative < 6.5
  - Positive ≥ 6.5

The PR Score positive/negative cut-off of 5.5 units was validated from a study of 761 samples using the PR536 antibody (immunohistochemistry) and another study of 517 samples using the PR636 antibody (immunohistochemistry). The standard deviation for the PR Score is less than 0.5 units.

**HER2 Score**
- **Negative**: 8.4
- Range: Patient
  - Negative < 10.7
  - Equivocal ≥ 10.7
  - Positive ≥ 11.5

The HER2 positive cut-off of 11.5 units, equivocal range from 10.7 to 11.4 units, and negative cut-off of < 10.7 units were validated from concordance studies of 761 samples using the HercepTest™ assay (immunohistochemistry) and another study of 568 samples using the PathVysion® assay (FISH). The standard deviation for the HER2 score is less than 0.5 units.

**References:**
1. ER Score based on quantitative ESR1 expression (estrogen receptor); PR Score based on quantitative PGR expression (progesterone receptor); HER2 Score based on quantitative SKBR3 expression.

**Laboratory Director:** Patrick Joseph, MD

This test was developed and its performance characteristics determined by Genomic Health, Inc. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing. This test is used for clinical purposes. It should not be used as investigational or for research. These results are not intended to aid in the ordering physician’s workup.

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The Recurrence Score® Result Reveals Individual Tumor Biology for ER+ Breast Cancer

Low Recurrence Score Disease
- Indolent
- Hormonal therapy–sensitive
- Minimal, if any, chemotherapy benefit

High Recurrence Score Disease
- Aggressive
- Less sensitive to hormonal therapy
- Large chemotherapy benefit

GUIDELINES

NCCN  ASCO  ESMO
THE ONCOTYPE DX® ASSAY IS THE ONLY MULTIGENE ASSAY INCORPORATED IN MAJOR GUIDELINES FOR PREDICTION OF ADJUVANT CHEMOTHERAPY BENEFIT

**NCCN Guidelines®**
- 0.5 cm, node negative, N1mi
- May be considered for select node-positive (1-3 LN) patients

**Quantifies risk of recurrence as a continuous variable and predicts responsiveness to both tamoxifen and chemotherapy**¹

**ASCO® Guidelines**
Node negative

**Predicts the risk of recurrence and may be used to identify patients likely to benefit from tamoxifen or chemotherapy**²

**St. Gallen Consensus**
Node negative, node positive

**Provides not only prognostic but also predictive information regarding the utility of cytotoxic therapy in addition to endocrine therapy**³

**NICE**
Node negative

**Recommended as an option for guidance of chemotherapy decisions in patients at intermediate risk* of distant recurrence**⁴

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ASCO is a trademark of the American Society of Clinical Oncology. NCCN and NCCN Guidelines are trademarks of the National Comprehensive Cancer Network. The guidelines do not endorse products or therapies.

*Intermediate risk of distant recurrence is defined as Nottingham Prognostic Index score above 3.4 or being at intermediate risk by other decision-making tools or protocols.*
Gene expression profiling and expanded IHC tests for guiding adjuvant chemotherapy decisions in early breast cancer management

- MammaPrint
- Oncotype DX
- IHC4
- Mammostrat.
Oncotype DX is recommended as an option for guiding adjuvant chemotherapy decisions for people with ER+/HER2-/LN− early breast cancer if:

- intermediate risk and
- Oncotype DX is likely to help in predicting the course of the disease and would therefore help when making the decision about prescribing chemotherapy and
- Confidential arrangement agreed with NICE.
NICE SEP 2013

GENE EXPRESSION PROFILING AND EXPANDED IHC TESTS FOR GUIDING ADJUVANT CHEMOTHERAPY DECISIONS IN EARLY BREAST CANCER MANAGEMENT

- Recommendation was based on intermediate risk of distant recurrence
- Nottingham Prognostic Index (NPI) score above 3.4.
- Protocols are also currently used in the NHS and these may also be used to identify people at intermediate risk.

- NICE encourages further data collection on the use of Oncotype DX in the NHS
Oncotype DX® is accepted for use in NHS Scotland as an option for guiding adjuvant chemotherapy decisions for patients who have:

- **ER positive, HER2 negative, lymph node negative breast cancer with an NPI of \( \geq 3.4 \) and in whom current risk stratification would lead to a recommendation for adjuvant chemotherapy but in whom the benefits of chemotherapy are considered uncertain by the multidisciplinary team.
Oncotype DX® testing should be discussed with such patients if the Oncotype DX® recurrence score (either intermediate or low risk) would influence the recommendation for systemic treatment, meaning that the patient would not proceed with adjuvant chemotherapy.
ECONOMIC IMPACT OF 21-GENE RECURRENCE SCORE TESTING ON EARLY-STAGE BREAST CANCER IN IRELAND

- The all Ireland Cooperative Oncology Research Group (ICORG) in combination with the National Cancer Control Program (NCCP)

- Reduction in adjuvant chemotherapy usage as a result of the test. The proportion of patients who received chemotherapy decreased from 87% to 30%.

The real life study undertaken by the Ontario Clinical Oncology Group (OCOG) Oncotype DX® Field Evaluation Study led to the avoidance of chemotherapy in 38% of patients.

The Christie NHS Foundation NHS Trust conducted a pilot study which concluded that there was a 66% reduced in the uptake of adjuvant

- 127/201 (63.2%) patients for all patients
- 60.3% for LN-ve disease
- 69.2% for LN+ve

Using the test was associated with significant cost savings.


• Impact of Oncotype DX breast Recurrence Score testing on adjuvant chemotherapy use in early breast cancer: Real world experience in Greater Manchester, UK, Loncaster et al, EJSO, Jan 2017
In September 2013, NICE recommended the use of Oncotype DX® for guiding adjuvant chemotherapy decisions in early breast cancer management in a defined cohort of patients. This cohort has been re-defined to ensure that it is only those patients that would derive benefit are tested.
THE IMPACT OF ONCOTYPE DX BREAST CANCER ASSAY RESULTS ON CLINICAL PRACTICE
A UK EXPERIENCE

358 patients tested

Low RS 185 (52%)
Intermediate RS 129 (36%)
High RS 42 (12%)

Low RS 4 + 10 (7.6%)
High RS 42 (100%)
Intermediate RS 46 (44.2%)

90 patients received chemotherapy (25.1%)

Royal Free London NHS, Sheffield NHS, Royal Marsden, Guy’s and St Thomas’ NHS, Velindre

Abstract 7, V Crolley, UKBCM, London Nov 2016
Mum convinced breast cancer chemo gave her leukemia shares story so other women can know risks

EILEEN Reid shares her story in a hope cancer specialists divulge the full extent of the risks associated with chemotherapy.
Breast cancer test which could spare patients chemotherapy available on NHS ... except in parts of Scotland

Eileen was diagnosed with breast cancer in 2011 and endured months of gruelling chemo. Three years later, she developed leukaemia – which she blames directly on her cancer treatment.

The mum of two said that, if she could turn back time, she would have refused chemo.

Eileen, from Glasgow’s west end, said: “My oncologist told me that of 100 women with breast cancer, only four require chemo – but they don’t know which four it is. That’s the kind of risk I think we ought to know about.”

The test, called Oncotype DX, can accurately predict the chances of a tumour returning once it has been removed by surgery.

And it can check whether a woman really needs chemotherapy.

Now, campaigners have called for all patients who would benefit from the test to have access to it.
Outcomes data in 50,000+ patients supporting clinical utility of the Oncotype DX® assay

<table>
<thead>
<tr>
<th>TAILORx Trial pN0</th>
<th>SEER Study pN0-pN1</th>
<th>Clalit Study pN0, pN1mi</th>
<th>WSG PlanB Trial pN0-pN1</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,626 Patients</td>
<td>&gt; 44,500 Patients</td>
<td>2,028 Patients</td>
<td>2,642 Patients</td>
</tr>
<tr>
<td>Recurrence Score result &lt; 11</td>
<td>Recurrence Score result &lt; 18</td>
<td>Recurrence Score result &lt; 18</td>
<td>Recurrence Score result ≤ 11</td>
</tr>
<tr>
<td>5-year distant recurrence-free survival rate of &gt; 99%</td>
<td>5-year breast cancer-specific survival rate of &gt; 99%</td>
<td>5-year distant recurrence-free survival and breast cancer-specific survival rates of &gt; 99%</td>
<td>5-year disease-free survival rate of 94%</td>
</tr>
</tbody>
</table>

> 50K Patients
The Recurrence Score® Result Identifies Those Patients that Derive the Greatest Benefit from Chemotherapy


RS: Recurrence Score result

PATIENTS WITH HIGH RS 28% absolute benefit from tamoxifen + chemotherapy
TAILORx: A CLINICAL TRIAL ASSIGNING INDIVIDUALIZED OPTIONS FOR TREATMENT (Rx)

Eligible 10,253 pts prospectively enrolled (2006-2010)

Published in NEJM 2015

Patients in Arm A were predominantly treated with AI (59%) and tamoxifen (34%)

RS: Recurrence Score® result

THE DISTRIBUTION OF RECURRENCE SCORE® RESULTS IN TAILORx IS REPRESENTATIVE OF THE COMMERCIAL EXPERIENCE

6897 patients
67.3%
Recurrence
Score 11-25
Arms B & C (randomized)

1626 patients
15.9%
Recurrence
Score <11
Arm A

1730 patients
16.9%
Recurrence
Score >25
Arm D

Commercial experience
- <11: 18%
- 11–25: 62%
- >25: 20%

Most patient characteristics and surgical treatment between arms were similar

<table>
<thead>
<tr>
<th></th>
<th>Arm A</th>
<th>Arm B/C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. eligible patients</strong></td>
<td>1626</td>
<td>6897</td>
</tr>
<tr>
<td><strong>Median age - yrs</strong></td>
<td>58</td>
<td>55</td>
</tr>
<tr>
<td><strong>Post-menopausal</strong></td>
<td>70%</td>
<td>64%</td>
</tr>
<tr>
<td><strong>Median tumor size - cm</strong></td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td><strong>Histologic grade</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>34%</td>
<td>29%</td>
</tr>
<tr>
<td>Intermediate</td>
<td>59%</td>
<td>57%</td>
</tr>
<tr>
<td>High</td>
<td>7%</td>
<td>14%</td>
</tr>
<tr>
<td><strong>ER expression</strong></td>
<td>&gt;99%</td>
<td>&gt;99%</td>
</tr>
<tr>
<td><strong>PgR expression</strong></td>
<td>98%</td>
<td>92%</td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumpectomy</td>
<td>68%</td>
<td>72%</td>
</tr>
<tr>
<td>Mastectomy</td>
<td>32%</td>
<td>28%</td>
</tr>
</tbody>
</table>

Differences between arms were clinically modest and would not allow a clinician to distinguish between patients having a low or mid-range Recurrence Score results.
Patients with Recurrence Score® Results <11 have less than 1% risk of distant recurrence at 5 years.


5 year DRFI Rate 99.3% (95% CI 98.7%, 99.6%)

n=1,626
Median follow-up 69 months
Patients with Recurrence Score® Results <11 may be safely spared adjuvant chemotherapy

No. of events: 88 iDFS events and 30 deaths within 5 years of registration, including 18 recurrences (10 distant as first event), 15 second primary breast cancers, 43 other second primary cancers, 12 deaths without another event.
**NEITHER AGE, SIZE NOR GRADE IMPACTED THE 5-YEAR DISTANT RECURRENCE RISK OR OVERALL SURVIVAL**

**Distant recurrence**

<table>
<thead>
<tr>
<th></th>
<th>DRFI, HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤50 vs 51-60 years</td>
<td>1.28 (0.12-4.22)</td>
<td>0.27</td>
</tr>
<tr>
<td>≤50 vs 61-75 years</td>
<td>3.49 (0.42-29.16)</td>
<td></td>
</tr>
<tr>
<td><strong>Tumor size</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;2 cm cm vs ≤2 cm</td>
<td>1.55 (0.38-6.31)</td>
<td>0.55</td>
</tr>
<tr>
<td><strong>Tumor grade</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2/3 vs 1</td>
<td>3.83 (0.48-30.69)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

**Event rates by grade**

<table>
<thead>
<tr>
<th></th>
<th>DRFI, % (95% CI)</th>
<th>OS, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All grades</strong></td>
<td>99.3 (98.7-99.6)</td>
<td>98.0 (97.1-98.6)</td>
</tr>
<tr>
<td><strong>Low grade</strong></td>
<td>99.8 (98.3-100)</td>
<td>98.7 (97.0-99.4)</td>
</tr>
<tr>
<td><strong>Intermediate grade</strong></td>
<td>99.0 (98.0-99.5)</td>
<td>97.9 (96.8-98.7)</td>
</tr>
<tr>
<td><strong>High grade</strong></td>
<td>100 (NC-NC)</td>
<td>97.3 (91.9-99.1)</td>
</tr>
</tbody>
</table>

HR, hazard ratio; NC, not calculated; DRFI, distant recurrence-free interval; OS, overall survival.

Many small tumors have intermediate to high recurrence score® disease.
Many younger patients have low recurrence score® disease.
SIGNIFICANT PROPORTION OF HIGH-GRADE TUMORS HAVE LOW RECURRENCE SCORE® DISEASE

## Beatson’s West of Scotland Data

<table>
<thead>
<tr>
<th>Category</th>
<th>Dates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experience Program</td>
<td>Oct 2015, Mar 2016</td>
</tr>
<tr>
<td>MPEP/MPC</td>
<td>Jan 2016</td>
</tr>
<tr>
<td>Contracts</td>
<td>Apr 2016, Dec 2016</td>
</tr>
</tbody>
</table>
EXPERIENCE PROGRAM (PILOT STUDY)  
OCT 2015 – MAR 2016

- Aim to evaluate the clinical utility of RS testing

- Primary objective: evaluate the impact of RS testing on adjuvant chemotherapy decision making

- Agreement between clinicians to follow NICE guidelines, ER+ve, Her2-negative

- The study included both node-negative and node-positive.

- Tests were requested even if the initial thought not to consider chemotherapy or unsure.
EXPERIENCE PROGRAM (PILOT STUDY)
OCT 2015 – MAR 2016

- Prospective data collection
- Clinical-pathological data and RS results
- Decision if the RS test is not available
- Choice of chemotherapy regieme
- Treatment choice after RS results
EXPERIENCE PROGRAM (PILOT STUDY)  
OCT 2015 – MAR 2016

RESULTS
56 TESTS REQUESTED FOR 53 PATIENTS
CLINICAL INFORMATION MISSING FOR 11

<table>
<thead>
<tr>
<th>Pre-test</th>
<th>Post-test</th>
<th>Total N=46</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>No</td>
<td>3 (6.5%)</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>7 (15%)</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>12 (26%) 11patients</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>7 (15%) 6 patients</td>
</tr>
<tr>
<td>Unsure</td>
<td>Yes</td>
<td>5 (11%)</td>
</tr>
<tr>
<td>Unsure</td>
<td>No</td>
<td>12 (26%) 11patient</td>
</tr>
</tbody>
</table>
Test Requests Per Practice

Average 11 days to receive results (6-29 days)

<table>
<thead>
<tr>
<th>Numbers of Tests Per Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lanarkshire</td>
</tr>
<tr>
<td>Victoria</td>
</tr>
<tr>
<td>GGH</td>
</tr>
<tr>
<td>Clyde</td>
</tr>
<tr>
<td>Stobhill</td>
</tr>
<tr>
<td>Ayrshyre</td>
</tr>
<tr>
<td>Forth Valley</td>
</tr>
</tbody>
</table>

136 tests for 132 patients
### Age Distribution

<table>
<thead>
<tr>
<th>Age</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 40</td>
<td>10</td>
</tr>
<tr>
<td>40 - 49</td>
<td>26</td>
</tr>
<tr>
<td>50-59</td>
<td>59</td>
</tr>
<tr>
<td>60 - 69</td>
<td>32</td>
</tr>
<tr>
<td>Over 70</td>
<td>9</td>
</tr>
</tbody>
</table>

Mean age: 54.8 years (range, 29-78)
### Tumour Size

<table>
<thead>
<tr>
<th>Tumour Size (mm)</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 10</td>
<td>5</td>
</tr>
<tr>
<td>10 – 20</td>
<td>46</td>
</tr>
<tr>
<td>21 – 30</td>
<td>57</td>
</tr>
<tr>
<td>31 – 40</td>
<td>18</td>
</tr>
<tr>
<td>41 – 50</td>
<td>6</td>
</tr>
<tr>
<td>Over 50</td>
<td>4</td>
</tr>
</tbody>
</table>

Mean tumour size: 24.9 mm (range, 8-110)
## Nodes

<table>
<thead>
<tr>
<th>Nodal Status</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>123</td>
</tr>
<tr>
<td>Micrometastases</td>
<td>11</td>
</tr>
<tr>
<td>Macrometastases</td>
<td>2</td>
</tr>
</tbody>
</table>
## Grade

<table>
<thead>
<tr>
<th>Grade</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>4</td>
</tr>
<tr>
<td>II</td>
<td>44</td>
</tr>
<tr>
<td>III</td>
<td>88</td>
</tr>
</tbody>
</table>
## ER STATUS

<table>
<thead>
<tr>
<th>ER status</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>115</td>
</tr>
<tr>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

One patient ER 6 scored 76: considered ER neg
ER 5 scored 62: considered ER neg
## PATIENTS CHARACTERISTICS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (Mean, range)</td>
<td>54.8, (29-78)</td>
</tr>
<tr>
<td>Presentation</td>
<td></td>
</tr>
<tr>
<td>Screening detected</td>
<td>34%</td>
</tr>
<tr>
<td>Tumour grade</td>
<td></td>
</tr>
<tr>
<td>Grade 1 [n, (%)]</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>44 (32%)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>88 (65%)</td>
</tr>
<tr>
<td>Tumour size, mm[mean, range]</td>
<td>24.9, (8-110)</td>
</tr>
<tr>
<td>NPI</td>
<td>4.2, (2.4-5.78)</td>
</tr>
<tr>
<td>PREDICT*</td>
<td>4.9% (0.8-11.2)</td>
</tr>
<tr>
<td>RS</td>
<td>20.9 (0-76)</td>
</tr>
</tbody>
</table>

* 81.6% mean 10 years survival with endocrine tx alone, (51.8%-94.4%)
Recurrence Score (RS) distribution by grade

Grade I (3%)
- 25% (1)
- 25% (1)
- 25% (1)

Grade II (32%)
- 9% (4)
- 30% (13)
- 34% (15)

Grade III (65%)
- 20% (18)
- 14% (12)
- 32% (28)
- 24% (21)
- 10% (9)

Legend:
- Red: >30
- Orange: 26-30
- Yellow: 18-25
- Green: 11-17
- Dark Green: 0-10
NPI VS RECURRENCE SCORE

$R^2 = 0.2650$
PREDICT VS RECURRENCE SCORES

$R^2 = 0.2069$
## Treatment by Patient Group in Relation to RS Scores

<table>
<thead>
<tr>
<th></th>
<th>Chemotherapy</th>
<th>No Chemotherapy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low RS</strong></td>
<td>1 (0.7%)</td>
<td>56 (41.2%)</td>
<td>57</td>
</tr>
<tr>
<td><strong>Intermediate RS</strong></td>
<td>23 (16.9%)</td>
<td>36 (26.5%)</td>
<td>59</td>
</tr>
<tr>
<td><strong>High RS</strong></td>
<td>20 (14.7%)</td>
<td>0 (0%)</td>
<td>20</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>44 (32.4%)</td>
<td>92 (67.6%)</td>
<td></td>
</tr>
</tbody>
</table>

RS, Recurrence Score (Low, <18; 18-30; High>=30)

RS*Chemotherapy Treatment = Significant association (p<0.001)
## Chemo Given

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>FEC-80</td>
<td>21</td>
</tr>
<tr>
<td>AC</td>
<td>4</td>
</tr>
<tr>
<td>FEC-D</td>
<td>9</td>
</tr>
<tr>
<td>TC</td>
<td>10</td>
</tr>
</tbody>
</table>

![Pie chart showing distribution of chemo given (FEC-80: 0.48, FEC-D: 0.23, TC: 0.20, AC: 0.09).](chart.png)
# Treatment by Patient Group in Relation to RS Scores

<table>
<thead>
<tr>
<th></th>
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</tr>
<tr>
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<td>136</td>
</tr>
</tbody>
</table>

RS, Recurrence Score (Low, <18; 18-30; High>=30)

For the intermediate group
- RS=18-24 6/30 (20%) received chemotherapy
- RS=25-30 17/23 (74%)
RED = RECEIVED CHEMOTHERAPY
## Recurrence Score vs Predict

<table>
<thead>
<tr>
<th></th>
<th>≤3%</th>
<th>&gt; 3%</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low score &lt;18</td>
<td>13</td>
<td>44</td>
<td>57 (41.9%)</td>
</tr>
<tr>
<td>Intermediate 18-30</td>
<td>15</td>
<td>44</td>
<td>59 (43.9%)</td>
</tr>
<tr>
<td>High &gt;30</td>
<td>2</td>
<td>18</td>
<td>20 (14.7%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>30 (22.0%)</td>
<td>106 (77.9%)</td>
<td></td>
</tr>
</tbody>
</table>

Predict score: 10 yr survival benefit chemotherapy (3rd generation)
Recurrence Score vs Predict

<table>
<thead>
<tr>
<th></th>
<th>≤3%</th>
<th>&gt; 3%</th>
<th>total</th>
</tr>
</thead>
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<tr>
<td>Total</td>
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<td></td>
</tr>
</tbody>
</table>

Predict score: 10 yr survival benefit chemotherapy (3rd generation)

Rs score reduced patients number receiving chemotherapy from 103 to 44

59/132 (44.7%) avoided chemotherapy
Assuming, prior to Oncotype testing, only those patients with a survival benefit of 3% or greater (PREDICT), would be likely to receive chemotherapy then this would equate to 103/132 patients (78%). 44/132 patients (33.3%) actually received chemotherapy after Oncotype Dx recurrence score, consistent with avoidance of chemotherapy in 44% of the entire cohort.

Interestingly, in this cohort 8/30 patients (26.7%) with minimal predicted chemotherapy benefit based on PREDICT did receive chemotherapy.
Recurrence Score vs Predict

<table>
<thead>
<tr>
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<th>&gt; 3%</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low score &lt;18</td>
<td>26</td>
<td>31</td>
<td>57 (41.9%)</td>
</tr>
<tr>
<td>Intermediate 18-30</td>
<td>29</td>
<td>30</td>
<td>59 (43.9%)</td>
</tr>
<tr>
<td>High &gt;30</td>
<td>9</td>
<td>11</td>
<td>20 (14.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>64 (47.1%)</td>
<td>72 (52.9%)</td>
<td></td>
</tr>
</tbody>
</table>

Predict score: 10 yr survival benefit chemotherapy (2nd generation)

Rs score reduced patients number receiving chemotherapy from 71 to 44

27 (20.5%) avoided chemotherapy
NOTE

12 cases RS score was requested when NPI<3.4
- 2/12 has PREDICT >3%
- Low RS 4/12
- Intermediate RS 7/12 then 3 received chemo
- High RS 1/12 then 1 received chemo

Lobular morphology ILC
- 11/19 low RS
- 8/19 intermediate
- None High risk
## Chemotherapy Usage by Clinical and Genomic Risk

<table>
<thead>
<tr>
<th>Predicted 10 Year Survival Benefit with Chemotherapy</th>
<th>Received Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3%</td>
<td>0/13</td>
</tr>
<tr>
<td>&gt;3%</td>
<td>1/44</td>
</tr>
<tr>
<td>&gt;5%</td>
<td>1/24</td>
</tr>
<tr>
<td>Low RS (&lt;18)</td>
<td>1/57 (1.8%)</td>
</tr>
<tr>
<td>Intermediate RS (18-30)</td>
<td>7/15</td>
</tr>
<tr>
<td></td>
<td>16/44</td>
</tr>
<tr>
<td></td>
<td>12/23</td>
</tr>
<tr>
<td></td>
<td>23/59 (39%)</td>
</tr>
<tr>
<td>High RS (&gt;30)</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>18/18</td>
</tr>
<tr>
<td></td>
<td>10/10</td>
</tr>
<tr>
<td></td>
<td>20/20 (100%)</td>
</tr>
<tr>
<td>Received chemotherapy</td>
<td>8/30 (26.7%)</td>
</tr>
<tr>
<td></td>
<td>35/106 (25.7%)</td>
</tr>
<tr>
<td></td>
<td>23/57 (40.6%)</td>
</tr>
<tr>
<td></td>
<td>44/136 (32.3%)</td>
</tr>
</tbody>
</table>

- Absolute improvement in 10 year overall survival with chemotherapy, calculated within PREDICT v1.2-v2
CONCLUSIONS

- In this cohort 44/132 (33.3%) of patients who had RS test received chemotherapy. Of patients likely to receive chemotherapy based on clinico-pathological features:
  - 69/104 (66.3%) patients with predicted chemotherapy benefit $\geq 3\%$ did not receive chemotherapy
  - 34/57 (59.6%) patients with predicted chemotherapy benefit $\geq 5\%$ did not receive chemotherapy
CONCLUSIONS

- Confidence in the test appears high with all high risk patients receiving chemotherapy and most low risk patients avoiding it.

- The intermediate category was divided in respect to chemotherapy decisions further results are awaited from the TAILORx trial as to the extent of benefit of chemotherapy in this group.
CONCLUSIONS

- **Budget impact**
  - It is an expensive test;
    - published commercial list price £2580
  - chemotherapy treatment is expensive
    - NICE health technology assessment £6181
      - (drug cost, administration and monitoring, treating adverse events, secondary prevention of NS)
- Ki-67 not available routinely at WOS
- Need for QPI Audit across networks
- audit dataset to measure decision impact and budget impact at a national level
AKNOWLEDGMENT

- Dr Alanna Morton (StR Clinical Oncology)
- Dr Sophie Barrett (Oncology Breast team Lead)
- Dr. Iain MacPherson
- Dr. Abdulla Alhasso
- Dr. Graeme Lumsden
- Dr. Judith Fraser
- Dr. Diane Ritchie
- Dr. Jonathan Hicks
- Dr. Hosney Yosef
- Dr. Stefan Nowicki
- Dr. Lucy Scott
- Dr. Iffet Rabnawaz
- Breast cancer specialist nurses